AMENDMENT OF THE SPECIFICATION

Please amend the specification as follows:

Please add the following new paragraph after the paragraph ending at page 2, line 4:

INCORPORATION BY REFERENCE OF SEQUENCE LISTING PROVIDED ON COMPACT DISCS

An electronic version on compact disc (CD-R) of the Sequence Listing is filed herewith in duplicate (labeled COPY 1 REPLACEMENT 10/27/2006 and COPY 2 REPLACEMENT 10/27/2006), the contents of which are incorporated by reference in their entirety. The computer-readable file on each of the aforementioned compact discs, created on October 27, 2006, is identical, 687 kilobytes in size, and titled 923SEQ.004.txt.

Please replace the paragraph beginning at page 1, line 14 with the following amended paragraph:

This application is related to corresponding International PCT application No. ~~attorney docket No. 37851-923PC~~ WO 04/022747, entitled RATIONAL DIRECTED PROTEIN EVOLUTION USING TWO-DIMENSIONAL RATIONAL MUTAGENESIS SCANNING. This application also is related to U.S. application Serial No. 10/658,834, entitled "RATIONAL EVOLUTION OF CYTOKINES FOR HIGHER STABILITY, THE CYTOKINES AND ENCODING NUCLEIC ACID MOLECULES ~~AND RELATED APPLICATIONS~~," filed the same day herewith; to U.S. Provisional Application Serial No. 60/457,135, entitled "RATIONAL EVOLUTION OF CYTOKINES FOR HIGHER STABILITY, ENCODING NUCLEIC ACID MOLECULES AND RELATED APPLICATIONS;" filed March 21, 2003, and to U.S. Provisional Application Serial No. 60/409,898, entitled "RATIONAL EVOLUTION OF CYTOKINES FOR HIGHER STABILITY, ENCODING NUCLEIC ACID MOLECULES AND RELATED APPLICATIONS," filed September 9, 2002, each to Rene Gantier, Thierry Guyon, Manuel Vega and Lila Drittanti. This application also is related to co-pending U.S. application Serial No. 10/022,249, filed December 17, 2001, entitled "HIGH THROUGHPUT DIRECTED EVOLUTION BY RATIONAL MUTAGENESIS," to Manuel Vega and Lila Drittanti.

Replace the paragraph beginning at page 7, line 29 with the following amended paragraph:

Figure 6(A) displays the sequence of the mature IFNα-2b (SEQ ID NO:1). Residues targeted by a mixture of proteases, including α-chymotrypsin (F, L, M, W, and Y), endoproteinase Arg-C (R), endoproteinase Asp-N (D), endoproteinase Glu-C (E), endoproteinase Lys-C (K), and trypsin (K, and R), are underlined and in bold lettering.

Replace the paragraph beginning at page 9, line 17 with the following amended paragraph:

Figure 12 illustrates the two-dimensional (2D) matrix representation of a protein sequence, wherein the vertical axis represents the amino acid present at the corresponding position indicated on the horizontal axis and the horizontal axis represents the amino acid position along the length protein sequence (such that the first cell corresponds to amino acid position No. 1, the second cell to amino acid position No. 2, etc.). The matrix always contains 20 cells in one direction (the amino acid type) and a variable number of position-cells depending on the size of the protein, the number of position-cells equaling the number of amino acids in the protein sequence. An exemplary protein sequence (SEQ ID NO:502) is shown above the matrix and within the matrix, such that those cells corresponding to the actual sequence of the protein are indicated with shaded squares.

Replace the paragraph beginning at page 40, line 22 with the following amended paragraph:

In an additional embodiment, once one protein within a family of proteins (e.g., IFNα-2b within the cytokine family) is optimized using the methods provided herein for generating LEAD mutants, is-HITs can be readily identified on the remaining proteins within the particular family by identifying the corresponding amino acid positions therein using a structural homology analysis (see, co-pending U.S. application Serial No. [[922]] 10/658,834, filed the same day herewith, based on U.S. Provisional Application Serial No. 60/457,135 and to U.S. Provisional Application Serial No. 60/409,898). The is-HITs identified in this manner then can be subjected to the next step of identifying replacing amino acids and further assayed to obtain LEADs or super-LEADs as described herein.